What is Claimed is:

1. A compound having the structure:

R"—OOOOH

 $R_0 \stackrel{\downarrow}{R}$

wherein R, R_0 , and R' are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldedyde linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2 , N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein R" is - CHY = CHX, or H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; and wherein X is H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; wherein Y is H or linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N-NR_4R_5$, wherein R_3 , R_4 and R_5 are independently H or a linear or branched alkyl; and wherein n is 0, 1, 2, or 3.

ΉΟ

2. The compound of claim 1 having the structure:

(CH₂)₃-OH.

A compound having the structure:

wherein R, R_0 , and R' are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldedyde linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2 , N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein R" is - CHY = CHX, or H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; and wherein X is H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; wherein Y is H or linear or branched chain alkyl; wherein Z is O, $N(OR_3)$ or $N-NR_4R_5$, wherein R_3 , R_4 and R_5 are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3.

4. The compound of claim 3 having the structure:

wherein R is H, methyl, ethyl, n-propyl, n-butyl or n-hexyl.

1-7-

A compound having the structure:

1 2

wherein R, R₀, and R' are independently H, linear or branched chain alkyl, optionally

substituted by hydroxy, alkoxy, carboxy, carboxaldedyde linear or branched alkyl or

cyclic acetal, fluorine, NR₁R₂, N-hydroximino, or N-alkoxyimino, wherein R₁ and R₂

are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein R" is -

CHY = CHX, or H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-

furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; and wherein X is H, linear or branched chain alkyl,

phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; wherein Y is H

or linear or branched chain alkyl; wherein Z is O, N(OR₃) or N-NR₄R₅, wherein R₃, R₄

and R₅ are independently H or a linear or branched chain alkyl; and wherein n is 0,

3

4 5

6

7 8

9 10

12 13

11

14 15

1 6. The compound of claim 5 having the structure:

1, 2, or 3.

2

3 4

wherein R is H, methyl, ethyl, n-propyl, n-butyl, n-hexyl or hydroxypropyl.

1

7. A compound having the structure:

15.

R' OH OH OH OH

wherein R, R_0 , and R' are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldedyde linear or branched alkyl or cyclic acetal, fluorine, NR_1R_2 , N-hydroximino, or N-alkoxyimino, wherein R_1 and R_2 are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein R" is - CHY = CHX, or H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; and wherein X is H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; wherein Y is H or linear or branched chain alkyl; wherein Z is O, N(OR₃) or N-NR₄R₅, wherein R₃, R₄ and R₅ are independently H or a linear or branched chain alkyl or alkoxy; and wherein n is 0, 1, 2, or 3.

Ĥ

8. A compound having the structure:

N ...

Н

9. A compound having the structure:

QR' QR'' X

33.4

wherein R' and R' are independently hydrogen, a linear or branched alkyl,

substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is oxygen, $(OR^*)_2$, $(SR^*)_2$, $-(O-(CH_2)_n-O)-$, $-(O-(CH_2)_n-S)-$ or $-(S-(CH_2)_n-S)-$; wherein R^* is a linear or branched alkyl, substituted or unsubstituted aryl or benzyl; wherein R_2B is a linear, branched or cyclic alkyl or substituted or unsubstituted aryl or benzyl boranyl moiety; and wherein n is 2, 3 or 4.

10. A compound having the structure:

wherein R´ and R´´ are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is oxygen, $(OR^*)_2$, $(SR^*)_2$, $-(O-(CH_2)_n-O)$ -, $-(O-(CH_2)_n-S)$ - or $-(S-(CH_2)_n-S)$ -; wherein R* is a linear or branched alkyl, substituted or unsubstituted aryl or benzyl; wherein R₂B is a linear, branched or cyclic alkyl or substituted or unsubstituted aryl or benzyl boranyl moiety; wherein Y is OH, linear or branched chain alkoxy, trimethylsilyloxy, t-butyldimethylsilyloxy or methyldiphenysilyloxy; and wherein n is 2, 3 or 4.

11. A compound having the structure:

wherein R´ and R´´ are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is oxygen, (OR)₂, (SR)₂, -(O-(CH₂)_n-O)-, -(O-(CH₂)_n-S)- or -(S-

- 8 (CH₂)_n-S)-; and wherein n is 2, 3 or 4.
- 1 12. The compound of claim 11 wherein R' is TBS, R' is TPS and X is (OMe)₂.
- 1 13. A compound having the structure:

wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is a halogen; wherein R" is H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; and wherein Y is H or linear or branched chain alkyl.; wherein R' is H, linear or branched chain alkyl, hydroxymethyl, hydroxypropyl, alkyl carboxaldehyde, alkyl carboxaldehyde linear or cyclic acetal; and X is a halide.

- 1 14. The compound of claim 13 wherein R is acetyl and X is iodo.
- 1 15. A compound having the structure:

wherein R´ and R´´ are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is oxygen, $(OR)_2$, $(SR)_2$, $-(O-(CH_2)_n-O)-$, $-(O-(CH_2)_n-S)-$ or $-(S-(CH_2)_n-S)-$; and wherein n is 2, 3 or 4.

1 16. A compound having the structure:

wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or

indolyl or 6-indolyl; and wherein Y is H or linear or branched chain alkyl.

unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is a halogen; wherein R' is H, linear or branched chain alkyl,

alkyl carboxaldehyde, alkyl carboxaldehyde linear or cyclic acetal; wherein R" is H,

linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-

ΤU

17. A compound having the structure:

wherein R is hydrogen, methyl, ethyl, n-propyl, n-hexyl, $\mathrm{CO}_2\mathrm{Et}$,

CH₂OH; or (CH₂)₃-OH; wherein R´ and R´´ are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted

aroyl or benzoyl; and wherein Z is hydrogen, or linear or branched chain alkyl.

18. A method of preparing a Z-haloalkene ester having the structure:

wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein R' is hydrogen, methyl, ethyl, n-propyl, n-hexyl,

which comprises

(a) oxidatively cleaving a compound having the structure:

under suitable conditions to form an aldehyde intermediate; and

(b) condensing the aldehyde intermediate with a halomethylene transfer agent under suitable conditions to form the Z-haloalkene ester.

- 1 19. The method of claim 18 wherein X is iodine.
- 1 20. The method of claim 18 wherein the halomethylene transfer agent is $Ph_3P = CR'I$ or $(Ph_3P+CHR'I)I^{-1}$
- 1 21. A method of preparing an optically pure compound having the structure:

wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises:

(a) condensing an allylic organometallic reagent with an unsaturated aldehyde having the structure:

under suitable conditions to form an alcohol, and, optionally concurrently therewith, optically resolving the alcohol to form an optically pure alcohol having the structure:

- (b) alkylating or acylating the optically pure alcohol formed in step (a) under suitable conditions to form the optically pure compound.
- 22. The method of claim 21 wherein the allylic organometallic reagent is an allyl(trialkyl)stannane.

- 1 23. The method of claim 21 wherein the condensing step is effected using a reagent comprising a titanium tetraalkoxide and an optically active catalyst.
- The method of claim 23 wherein the optically active catalyst is S(-)BINOL.
 - 25. A method of preparing an open-chain aldehyde having the structure:

wherein R´ and R´´ are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises:

(a) cross-coupling a haloolefin having the structure:

wherein R is a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, trialkylsilyl, aryldialkylsilyl, diarylalkylsilyl, triarylsilyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, and X is a halogen, with a terminal olefin having the structure:

 $\omega_{j_{1}}$

OR' OR"
CH(OR'")2

wherein $(OR''')_2$ is $(OR_0)_2$, $(SR_0)_2$, $-(O-(CH_2)_n-O)-$, $-(O-(CH_2)_n-S)-$ or $-(S-(CH_2)_n-S)-$ where R_0 is a linear or branched alkyl, substituted or unsubstituted aryl or benzyl; and wherein n is 2, 3 or 4, under suitable conditions to form a cross-coupled compound having the structure:

wherein Y is CH(OR*)₂ where R* is a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl; and deprotecting the cross-coupled compound formed in step (a) under suitable conditions to form the open-chain compound.

26. A method of preparing an epothilone having the structure:

H O O O OH OH

which comprises:

(a) deprotecting a cyclized compound having the structure:

wherein R´ and R´´ are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, under suitable conditions to form a deprotected cyclized compound and oxidizing the deprotected cyclized compound under suitable conditions to form a desoxyepothilone having the structure:

and

- (b) epoxidizing the desoxyepothilone formed in step (a) under suitable conditions to form the epothilone.
- 27. A method of preparing an epothilone precursor having the structure:

wherein R_1 is hydrogen or methyl; wherein X is O, or a hydrogen and OR´´, each singly bonded to carbon; and wherein R_0 , R´ and R´´ are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises

(a) coupling a compound having the structure:

14

15

16 17

18 19 20

21 22

23

1

2

1

wherein R is an acetyl, with an aldehyde having the structure:

wherein Y is oxygen, under suitable conditions to form an aldol intermediate and optionally protecting the aldol intermediate under suitable conditions to form an acyclic epthilone precursor having the structure:

Ę.

- (b) subjecting the acylic epothilone precursor to conditions leading to intramolecular olefin metathesis to form the epothilone precursor.
- 28. The method of claim 27 wherein the conditions leading to intramolecular olefin metathesis require the presence of an organometallic catalyst.
- 29. The method of claim 27 wherein the catalyst is a Ru or Mo complex.
- 1 30. A pharmaceutical composition for treating cancer comprising a compound of claim 1,

1

15

16

17

2324252627

- 3, 5, 7, or 8 and a pharmaceutically suitable carrier.
- A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound of claim 1, 3, 5, 7 or 8 and a pharmaceutically suitable carrier.
- 1 32. The method of claim 31 wherein the cancer is a solid tumor.
- 1 33. The method of claim 31 wherein the cancer is breast cancer.
 - 34. A method of preparing a Z-iodoalkene ester having the structure:

wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises

(a) coupling a compound having the structure:

with a methyl ketone having the structure:

wherein R´ and R´´ are independently a linear or branched alkyl,

 alkoxyalkyl, substituted or unsubstituted aryl or benzyl, under suitable conditions to form a compound having the structure:

(b) treating the compound formed in step (a) under suitable conditions to form a Z-iodoalkene having the structure:

and

- (c) deprotecting and acylating the Z-iodoalkene formed in step (b) under suitable conditions to form the Z-iodoalkene ester.
- 35. A method of preparing an open-chain aldehyde having the structure:

wherein R is a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted

aryloxyalkyl, trialkylsilyl, aryldialkylsilyl, diarylalkylsilyl, triarylsilyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; and wherein R´ and R´´ are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises:

(a) cross-coupling a haloolefin having the structure:

wherein X is a halogen, with a terminal hydroborane having the structure:

wherein R_2^*B is a linear, branched or cyclic alkyl or substituted or unsubstituted aryl or benzyl boranyl moiety; wherein Y is $(OR_0)_2$, $(SR_0)_2$, $(O-(CH_2)_n-O)-$, $-(O-(CH_2)_n-S)-$ or $-(S-(CH_2)_n-S)-$ where R_0 is a linear or branched alkyl, substituted or unsubstituted aryl or benzyl; and wherein n is 2, 3 or 4, under suitable conditions to form a cross-coupled compound having the structure:

1 2

and

- (b) deprotecting the cross-coupled compound formed in step (a) under suitable conditions to form the open-chain aldehyde.
- 36. The method of claim 35 wherein R is acetyl; R' is TBS; R'' is TPS; R*₂B is derived from 9-BBN; and Y is (OMe)₂.
- 1 37. A method of preparing a protected epothilone having the structure:

wherein R´ and R´´ are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkyl-arylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzyl, which comprises:

(a) monoprotecting a cyclic diol having the structure:

11

12 13

under suitable conditions to form a cyclic alcohol having the structure:

14

15

16

17

and

- (b) oxidizing the cyclic alcohol formed in step (a) under suitable conditions to form the protected epothilone.
- 1 38. The method of claim 37 wherein R' and R" are TBS.
- 1 39. A method of preparing an epothilone having the structure:

N H O O OH OH OH

which comprises:

(a) deprotecting a protected cyclic ketone having the structure:

wherein R´ and R´´ are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, under suitable conditions to form a desoxyepothilone having the structure:

16

17

18

1

2

3

4 5

6

7

H O O OH OH

and

(b) epoxidizing the desoxyepothilone formed in step (a) under suitable conditions to form the epothilone.

1 40. The method of claim 39 wherein R' and R'' are TBS.

41. A method of preparing a cyclic diol having the structure:

wherein R^{*} is a hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises:

(a) cyclizing an open-chain aldehyde having the structure:

11 12

13 14

15

16 17

18

wherein R is a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, trialkylsilyl, aryldialkylsilyl, diarylalkylsilyl, triarylsilyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; and wherein R´´ is a hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl under suitable conditions to form an enantiomeric mixture of a protected cyclic alcohol having the structure:

19 20

21 (b)

(c)

22

23

24

25

26

optionally isolating and oxidizing the α -alcohol formed in step (a) under suitable conditions to form a ketone and thereafter reducing the ketone under suitable conditions to form an enantiomeric mixture of the protected cyclic alcohol comprising substantially the β-alcohol; and

said mixture comprising an α - and a β -alcohol component;

treating the protected cyclic alcohol formed in step (a) or (b) with a deprotecting agent under suitable conditions to form the cyclic diol.

- 42. The method of claim 41 wherein R' is TBS and R'' is TPS.
- 1 43. A purified compound having the structure: 2 3 4

wherein R is hydrogen, methyl, ethyl, propyl, hexyl, hydroxymethyl or hydroxypropyl; wherein X is O; and wherein R_0 , R´ and R´´ are independently hydrogen or acetyl.

1 44. A purified compound having the structure:

wherein R_1 is hydrogen, methyl, ethyl, propyl, hexyl, hydroxymethyl or hydroxypropyl; wherein X is O; and wherein R_0 , R´ and R´´ are independently hydrogen or acetyl.

長

45. A composition comprising an amount of the compound of claim 1, 2, 3, 4, 5, 6, 7, 8, 43 or 44 effective to inhibit the growth of multidrug resistant cells and a

pharmaceutically acceptable carrier.

3

1 The composition of claim 45, further comprising an amount of a cytotoxic agent. 46. 1 The composition of claim 46, wherein the cytotoxic agent is an anticancer agent. 47. 1 The composition of claim 47, wherein the anticancer agent is adriamycin. 48. The composition of claim 47, wherein the anticancer agent is vinblastin. 1 49. The composition of claim 47, wherein the anticancer agent is paclitaxel. 1 50. 1 51. The composition of claim 45, wherein the effective amount of the compound is 2 between about 0.01 mg/kg to about 25 mg/kg of body weight. A method of inhibiting the growth of multidrug resistant cells comprising contacting 1 52. 2 the multidrug resistant cells with an amount of the compound of claim 1, 2, 3, 4, 5, 3 6, 7, 8, 43 or 44 effective to inhibit the growth of multidrug resistant cells in 4 combination with a pharmaceutically acceptable carrier. 1 53. The method of claim 52, further comprising administering an amount of a cytotoxic 2 agent. 1 54. The method of claim 53, wherein the cytotoxic agent is an anticancer agent. 1 55. The method of claim 54, wherein the anticancer agent is adriamycin. 1 56. The method of claim 55, wherein the anticancer agent is vinblastin. 1 57. The method of claim 55, wherein the anticancer agent is paclitaxel. 1 58. The method of claim 55, wherein the effective amount of the compound is between 2 about 0.01 mg/kg to about 25 mg/kg of body weight.